

REMARKS

Applicant respectfully submits this Preliminary Amendment and Information Disclosure Statement in connection with the filing of this Continuation/Divisional Application based upon copending application U.S.S.N. 09/309,947, filed 11 May 1999.

The Title of the Invention has been amended to reflect the claims submitted herein, each of which is fully supported by the original disclosure. Entry of this amendment is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

INFORMATION DISCLOSURE STATEMENT

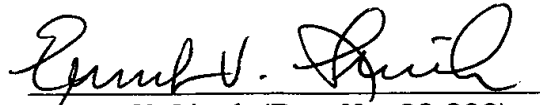
In accordance with the provisions of 37 C.F.R. §§1.56 and 1.97, Applicant herewith submits the publications and/or patents shown on the attached form PTO-1449, for consideration by the Examiner in connection with the examination of the above-identified patent application.

It is respectfully requested that each of the documents shown on the attached form(s) PTO-1449 be made of record in this application. Copies of these documents are in the file of the parent application, Serial No. 09/309,947, filed 11 May 1999, and are thus not being resubmitted herein.

Early examination and allowance of the present application are respectfully solicited.

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TO5001-2581/660

Respectfully submitted,



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Date: October 3, 2001

Document No. 14005

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**VERSION WITH MARKINGS TO SHOW CHANGES
MADE**

IN THE TITLE:

The Title was amended as follows:

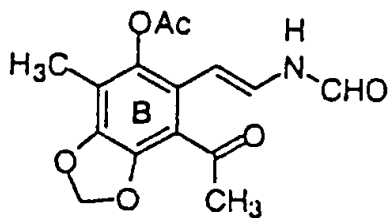
Metabolites of Ecteinasidin 743 Formed by Human Cytochrome CYP3A4

IN THE CLAIMS:

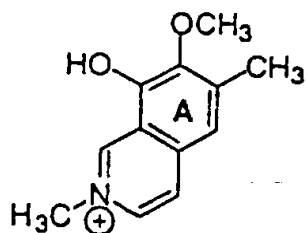
Original claims 1-16 were canceled.

New claims 17-40 have been added, as follows:

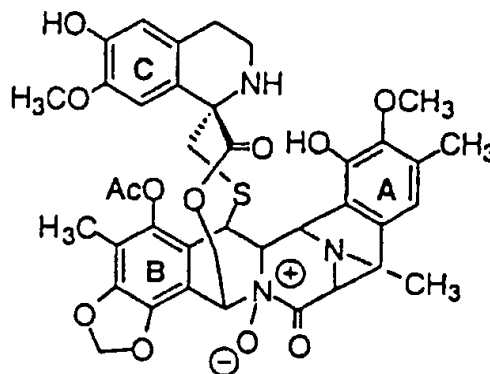
-- 17. (New) Metabolites of Ecteinasidin 743 formed by human cytochrome CYP3A4, said metabolites being selected from the group consisting of:



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-- 18. (New) The Ecteinasidin 743 metabolite of Claim 17, designated herein as ETM-305.--

-- 19. (New) The Ecteinasidin 743 metabolite of Claim 17, designated herein as ETM-204.--

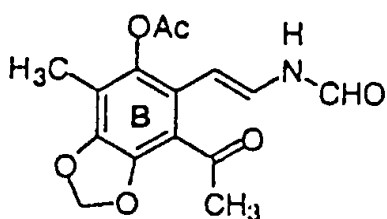
-- 20. (New) A pharmaceutical composition comprising one or more of the Eceteinasidin 743 metabolites of Claim 17 and a pharmaceutically acceptable diluent, excipient or carrier.--

-- 21. (New) The pharmaceutical composition of Claim 20, wherein the Ecteinasidin 743 metabolite is designated herein as ETM-305.--

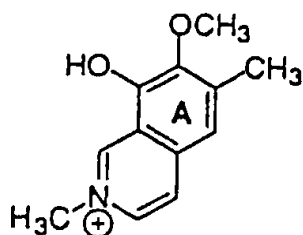
-- 22. (New) The pharmaceutical composition of Claim 20, wherein the Eceteinasidin 743 metabolite is designated herein as ETM-204.--

-- 23. (New) A method of treating mammalian leukemia in patients in need of such treatment, said method comprising administering an effective amount of a metabolite of Ecteinasidin 743 formed by human cytochrome CYP3A4 to said patient in unit dosage form, said metabolite being selected from the group consisting of:

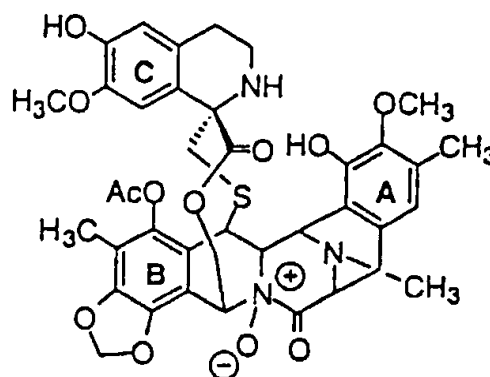
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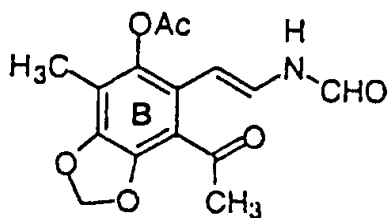
or mixtures thereof.--

-- 24. (New) The method of claim 23, wherein the Ecteinasidin 743 metabolite is designated herein as ETM-305.--

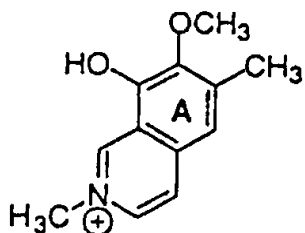
-- 25. (New) The method of Claim 23, wherein the Ecteinasidin 743 metabolite is designated herein as ETM-204.--

-- 26. (New) The method of Claim 23, wherein the Ecteinasidin 743 metabolite is designated herein as ETM-775.--

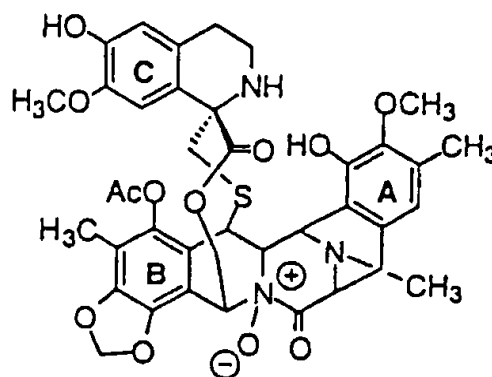
-- 27. (New) A method of treating mammalian lung carcinoma in patients in need of such treatment, said method comprising administering an effective amount of a metabolite of Ecteinasidin 743 formed by human cytochrome CYP3A4 to said patient in unit dosage form, said metabolite being selected from the group consisting of:



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or mixtures thereof.--

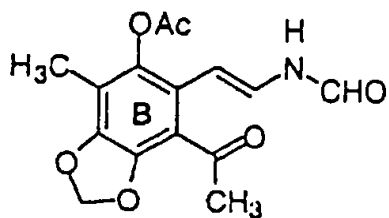
-- 28. (New) The method of Claim 27, wherein the Ecteinasidin 743 metabolite is designated herein as ETM-305.--

-- 29. (New) The method of Claim 27, wherein the Ecteinasidin 743 metabolite is designated herein as ETM-204.--

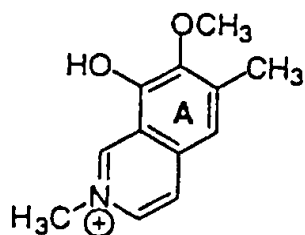
-- 30. (New) The method of Claim 27, wherein the Ecteinasidin 743 metabolite is designated herein as ETM-775.--

-- 31. (New) A method of treating mammalian colon adenocarcinoma in patients in need of such treatment, said method comprising administering an effective amount of a metabolite of Ecteinasidin 743 formed by human cytochrome CYP3A4 to said patient in unit dosage form, said metabolite being selected from the group consisting of:

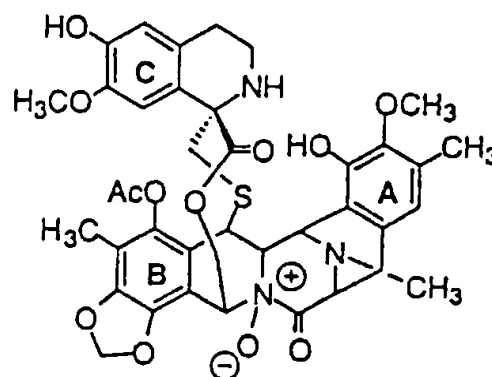
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or mixtures thereof.--

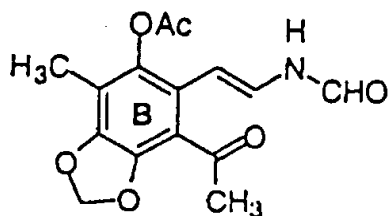
-- 32. (New) The method of Claim 31, wherein the Ecteinasidin 743 metabolite is designated herein as ETM-305.--

-- 33. (New) The method of Claim 31, wherein the Ecteinasidin 743 metabolite is designated herein as ETM-204.--

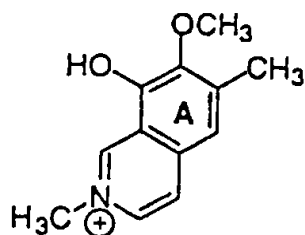
-- 34. (New) The method of Claim 31, wherein the Ecteinasidin 743 metabolite is designated herein as ETM-775.--

-- 35. (New) A method of treating mammalian malignant melanoma in patients in need of such treatment, said method comprising administering an effective amount of a metabolite of Ecteinasidin 743 formed by human cytochrome CYP3A4 to said patient in unit dosage form, said metabolite being selected from the group consisting of:

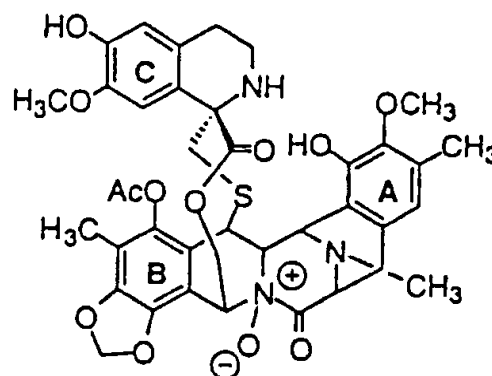
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or mixtures thereof.--

-- 36. (New) The method of claim 35, wherein the Ecteinasidin 743 metabolite is designated herein as ETM-305.--

-- 37. (New) The method of Claim 35, wherein the Ecteinasidin 743 metabolite is designated herein as ETM-204.--

-- 38. (New) The method of Claim 35, wherein the Ecteinasidin 743 metabolite is designated herein as ETM-775.--

-- 40. (New) A method of assaying the human cytochrome CYP3A4 metabolism of Ecteinasidin 743, comprising monitoring a test sample for the presence of one or more metabolites selected from the group consisting of ETM-204, ETM-305 and ETM-775.--

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